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Dry powder coating in a modified wurster apparatus

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Abstract

The results of dry coating of pharmaceutical materials (micro-particles), carried out in spout-fluid bed apparatus, designed by the authors are presented in the paper. The design has been developed starting from the Wurster conception device. The examination consisted of the determination of the optimal composition of coating mixture-powder to plasticizer proportion, as well as the determination of basic process parameters (flow rates of individual streams). Resistance of coating on the conditions in gastrointestinal tract was chosen as optimization criterion. The purpose of the process is to defend an active substance placed in a core from the surroundings in the stomach. This active substance should be excellent dissolved only just in the small intestine (in case of an intestine medicine application).

Keywords: Spout-fluid bed; dry powder coating; wurster apparatus

Nomenclature

c	methylene blue concentration	(mg/l)
t	time	(s)

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1. Introduction

Coating means putting an envelope on a core of tablet (microparticle) and it is commonly applied in pharmaceutical, food and chemical industries. Many times, this process is decisive in creating the needed properties of the commercial product [1].

The cores could be coated by the use of a sugar envelope, mainly saccharose (pills) or by multi-molecular substances possessing coating abilities (coated tablets). Applying coating, it is possible to protect active component from the activity of atmospheric agents (oxygen, carbon dioxide, light and humidity). It is also possible to get esthetic look and at the same time to mask odorous smell and taste of the active substances.

The coating protects the carrier from the loss of volatile components, that exist in it. It is also possible to get the effect of controllable dissolution of a medicine, in determined position of gastrointestinal tract (tablets dissolved in the gut), applying coating with the substances, which solubility depend on the pH in the environment [2].

The oral medicines with prolonged activity are used to assure constant, sufficiently high concentration of active substance in a human organism, for a long time e.g. 24 h [3]. The most important, in such an instance, is obtaining practically, a retarded absorption, by lowering the release speed of an active substance from the medicine. Coating enables, in that case, the separation of the initializing and sustaining doses actions. Sustaining dose is placed in the core of a medicine tablet and coated with an envelope, which is not dissolved in the gastric acid. The outer layer of the medicine tablet consists of a coat, which contains initializing dose, which dissolves in an acid medium. According to that, initializing dose is released immediately in the stomach and the sustaining dose acts only, after envelope dissolving, in the small intestine. The active substance could be released from the core once or in relevant periods of time.

The main disadvantage of classical film coating methods with the use of water, which supplant organic solvents, is high concentration of water in the final product. In the case of coating of medicines or other biologically active products, humidity could cause the product destruction or its inactivation [4]. In connection with that, it is necessary to dry the product gently for a long time, which increases the costs and lengthens the time of the whole process [2]. The solutions and suspensions of the coating substance possess high viscosity, which could cause both clogging of the nozzle and an agglomeration of the coating particles [5].

The solution of those problems is the dry coating method, in which the application of whatever liquids is completely or partially eliminated. Since nineties of XX century, different methods of dry coating have been investigated, considering their possibility of an application in the pharmaceutical industry. Although there has been potential possibility of those methods application, only few have been implemented in the industry [2, 6].

The basic disadvantage of those methods is comparatively a large loss of a valuable coating substance, which is blown away in the case of the fluidized-bed apparatus application. Unfortunately, the coating substance separated in a gas-solids separator could not be used again, because of its contamination by the plasticizer.

Among many known devices applied for particles coating, a spout-fluid bed apparatus, with a spraying nozzle located at the lower part of a bed are considered as an optimal construction [1]. There is great chance of solid particles collision with droplets of coating solution in that system, high process efficiency and short drying time. But there is also great risk of the bed agglomeration, just above the nozzle, because of high concentration of the wet particles [7]. Certain modification of this design is Wurster apparatus [8]. Wurster apparatus is constituted by a spouted bed apparatus with a draft tube and an additional air stream

fluidizing the bed (spout-fluid bed system). This type of apparatus is considered as the best in case of periodic coating of fine granular materials [1, 9].

The devices applied for dry coating are mostly redesigned classical apparatuses, which were applied for wet coating. In connection with that, such devices exhibit several disadvantages in dry coating process, as for example a considerable loss of the feedstock [2, 4].

The purpose of this work was an examination of the spout-fluid bed apparatus constructed by the authors, and which constitutes the development of Wurster conception. The apparatus was applied in the process of dry coating for the purpose of getting suitable coat, that could be used in a production of intestinal medicines. The device should significantly shorten the process time of dry coating, by increase of the speed of the particles circulation.

2. Research installation

The research work was done in the installation presented in Fig.1 and described in detail in the patent applications [10,11]. The main element of this installation was modified Wurster apparatus (9). After compression (1) the air was pushed to the column through the cooling device (2), set of filters (3), heater (4), and control panel (5), where the flow rates of specific streams were indicated and adjusted. The powder was taken from the tank (8) and transported to the powder nozzle by the use of the pneumatic device, which was supplied with compressed air. The plasticizer was pumped from the tank (7), by means of the peristaltic pump (6), to the atomizer, which was supplied with compressed air.

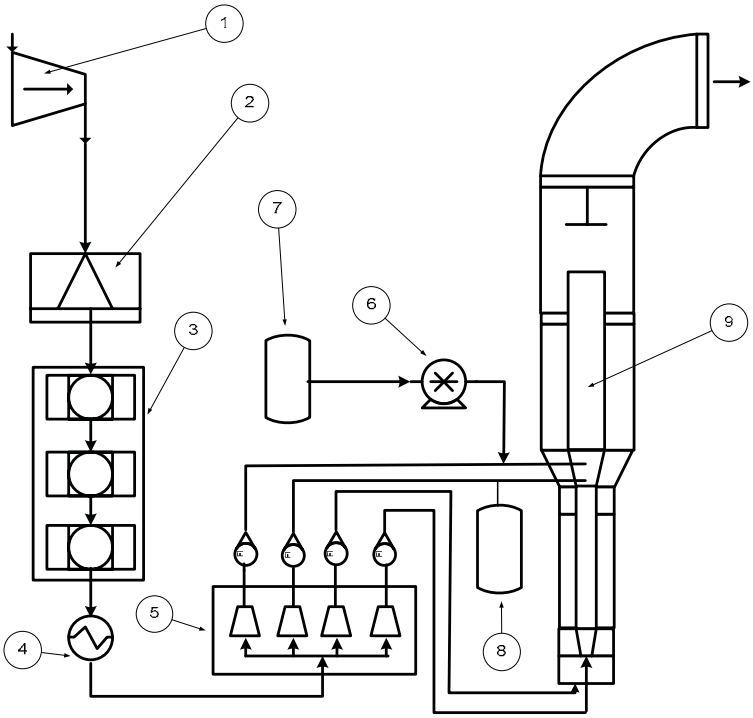

Fig. 1. Research installation: 1-compresor, 2-cooling device, 3-set of filters, 4-heater, 5-control panel, 6-peristaltic pump, 7-plasticizer tank, 8-powder tank, 9-spout-fluid bed column

The column (Fig.2) consisted of three main, cylindrical segments, a cone (Fig.2 - B) and the nozzles introducing an air, a plasticizer and also a coating substance. Above and below the lower segment, there were aluminum rings, equipped with the openings, which served for loading and collection of the particles (coated cores). Each of the segments possessed double walls, which allowed thermostating the apparatus. The outer wall was made of polycarbonate, and the inner one of the glass.

The draft tubes were situated in the axis of the segments, and connected together by the aluminum clamps. In the axis of the cone, connecting lower segment with the middle one, there were nozzles atomizing plasticizer and powder, which coated the cores. The upper segment was equipped with deflector (Fig.2- D), which limited particles blowing out of the installation.

The particles, poured into the apparatus, dropped freely to the bottom of the lower segment (Fig.2 - C). When the flow of the spouting gas was initiated, the particles were sucked and accelerated to the proper circulation velocity. It was possible, at this place to introduce the plasticizer, that lowered the glass transition temperature of the powder. The layer created on the particle surface was formed during the pneumatic transport in the middle segment. The cores leaving the draft tube created the fountain in the upper segment. They rebounded from the deflector, were directed to the annular zone, fell to the bottom and they were sucked again in the entrainment zone.

In the annular zone of the device, the material was additionally fluidized by means of the air, which was fed around the jet pump in the lower segment, which prevented sticking of the fine, electrically charged particles. The jet pump application for the spouting gas distribution, enabled fast circulation of the particles. Thanks to that, the time of the process was apparently shortened. The gas, that accelerated the particles, flowed through the elbow to the section of the bag filter, where it was cleaned from the blown material (the particles and the coating substance).

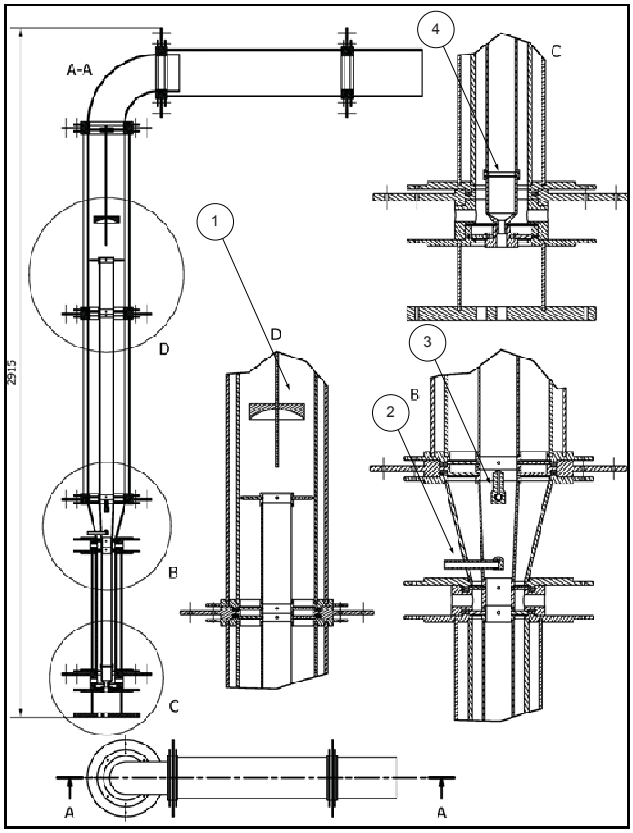

Fig. 2. Scheme of apparatus used in the investigation: 1 – deflector, 2 – powder nozzle, 3 – plasticizer nozzle, 4 – jet pump.

3. Materials

Cellets® 500 particles, made of crystalline cellulose, with the diameter 500 – 710 μm and the density 0.8 g/cm^3, produced by Syntapharm were used as the cores.

Hydroxypropyl methylcellulose acetate succinate produced by ShinEtsu and sold under the name of AQOAT was used as the coating agent. Fraction AS-MF, which dissolves at pH higher than 6 was applied in examination. Triethyl citrate was used as the plasticizer.

It is a common set of the materials used for intestine medicine production [2, 5].

The buffers: acidic (pH~1) and alkaline (pH~8) were used during evaluation of the strength of the created coating.

As a model substance, that simulates an active ingredient of intestine medicine, methylene blue was used for dyeing of the white cores.

4. Coating by „in vitro" method

Series of examinations „in vitro" were proceeded in purpose of getting optimal plasticizer to coating powder proportion, before carrying out the process of dry coating in Wurster apparatus. Relevant quantity (0.1-0.9 ml) of triethyl citrate and AQOAT (0.336-1.623 g) were added to 10 g of dyed cores.

The whole material was mixed carefully, and 5 g of the product was thermally cured in the dryer. The curing process was carried out for 45 minutes at temperature 60 ^{o}C. After that, the evaluation of obtained coatings was done. 1 g of the cured and uncured particles was placed separately in acidic buffer and then in alkaline buffer with temperature close to human body temperature (37 ^{o}C). The process of dissolution was carried out for 15 minutes and during that time samples of the solution were taken at determined periods of time. Spectrophotometer was used for the determination of methylene blue concentration in the samples. The methylene blue concentration in the acidic buffer should be the lowest possible, and the highest in the alkaline buffer.

The dissolution curves for the best series of examination are presented below.

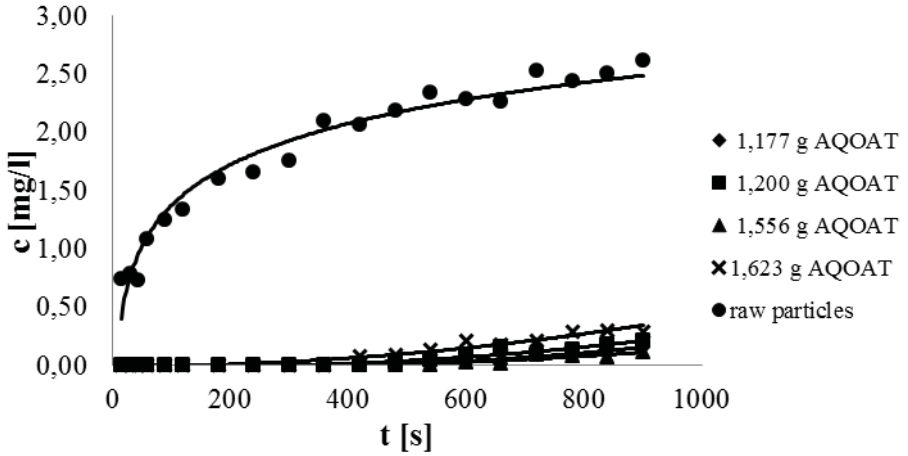

Fig. 3. Methylene blue concentration in the acidic solution as a function of time for the constant quantity of plasticizer (0.9 ml) for the different amount of AQOAT, added to 10 g of cured particles.

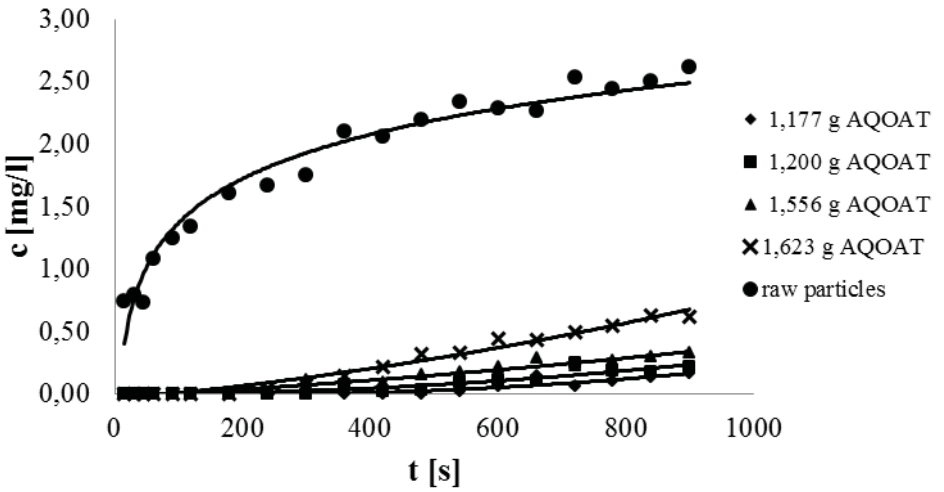

Fig. 4. Methylene blue concentration in the acidic solution as a function of time for the constant quantity of plasticizer (0.9 ml) for the different amount of AQOAT, added to 10 g of not cured particles.

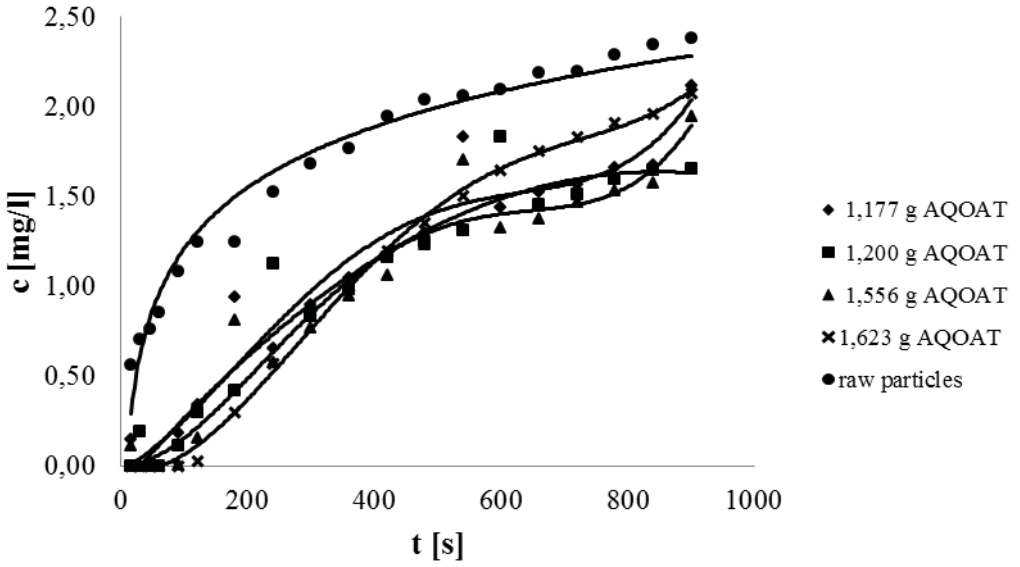

Fig. 5. Methylene blue concentration in the alkaline buffer as a function of time for the constant quantity of plasticizer (0.9 ml) for the different amount of AQOAT, added to 10 g of cured particles.

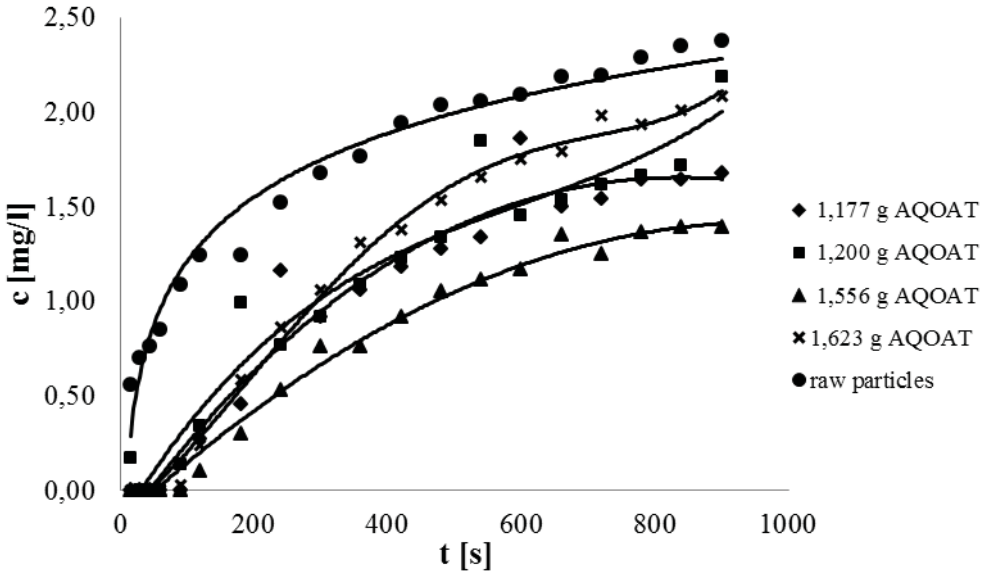

Fig. 6. Methylene blue concentration in the alkaline buffer as a function of time for the constant quantity of plasticizer (0.9 ml) for the different amount of AQOAT, added to 10 g of not cured particles.

The dissolution of the coating in an acidic environment decreases with the growth of AQOAT quantity up to 1.556 g for cured samples, with predetermined quantity of the plasticizer (0.9 ml) (Fig.3).

This is optimal value. Created coating is tight and possesses sufficient thickness. When the quantity of AQOAT grows the dissolution of the coating also grows, because the quantity of the triethyl citrate is too small to bind the added powder, and it goes to the solution. AQOAT does not influence significantly the dissolution, in case of cured particles and alkaline buffer application (Fig.5.). The curing causes the drop of the dissolution both in the acidic and alkaline environment (Fig. 3 and Fig. 5), but the concentration in the alkaline environment is satisfactory (Fig. 5). The created coating is fixed in this process, and the components homogenize into uniform layer.

On the basis of "in vitro" examination, optimal composition of coating mixture was set: 0.09 ml of the plasticizer, 0.1556 g of the powder for 1 g of particles.

5. Coating in the column

The next stage of the investigation were experiments in the column. 200 cm^3 of dyed particles was poured into the column. That was maximal amount of the material that could be spouted with the compressor applied in the investigation. The flow rates of the main stream and the additional stream of the air were constant and amounted: 424 and 87 l/min. respectively. The flow rates of coating powder and plasticizer were used as variable parameters. The air temperature at the inlet of the column was 45^oC (maximal possible value for the applied air flow rates). Thanks to that, an introductory thermal curing of the created coating layer followed. The time of process was selected specifically to get the optimal quantity of the plasticizer added to the column, which was established during "in vitro" examination (0.09 ml/1 g particles). Taking into consideration the fact that the curing of the product in the column could be insufficient (because of too low temperature), part of the product was cured additionally at the temperature of 60^oC for 45 minutes in the cabinet dryer.

The loss of feedstock (plasticizer and powder) was determined by weighing. The quality of the product was evaluated applying the methods presented in the previous chapter.

The investigation shows, that the plasticizer should be introduced with minimal flow rate of the peristaltic pump used in experiments (1 ml/min). When higher values of the plasticizer flow rate was used, the particles conglutinated quickly (especially in the cone with nozzles and in the bottom of the apparatus) and the circulation was stopped. The powder should be introduced with maximal flow rate. Applying lower flow rates, there were partial clogging of the feeding device, the quantity of powder feed diminished, and it influenced the quality of the product. Besides that, the large quantity of the powder prevented particles agglomeration.

When the conditions presented above were accomplished, the quality of the product was good (Fig.7 and Fig.8), however there was significant level of material loss (about 20%).

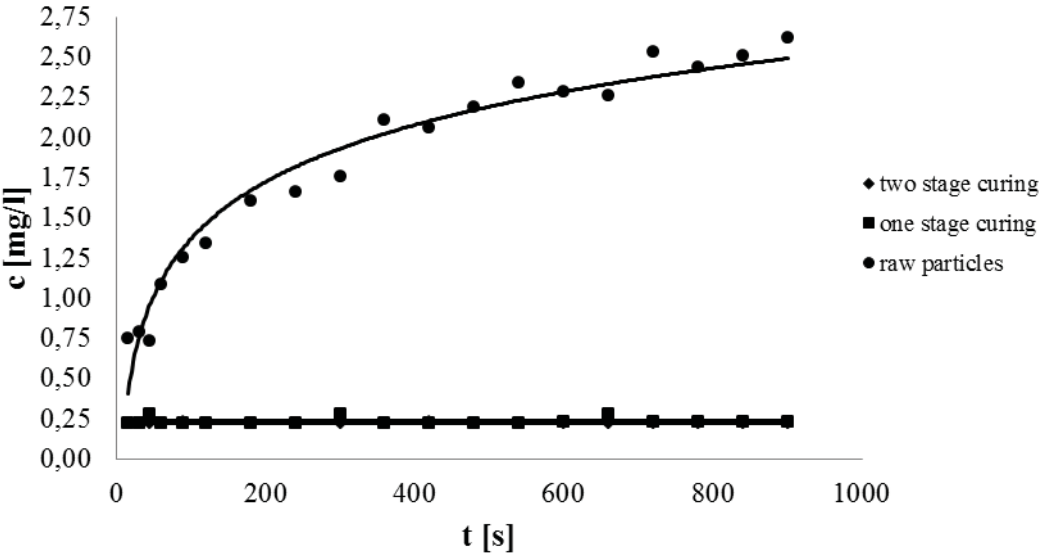

Fig. 7. Methylene blue concentration as a function of time for an example product obtained in the column (acidic environment).

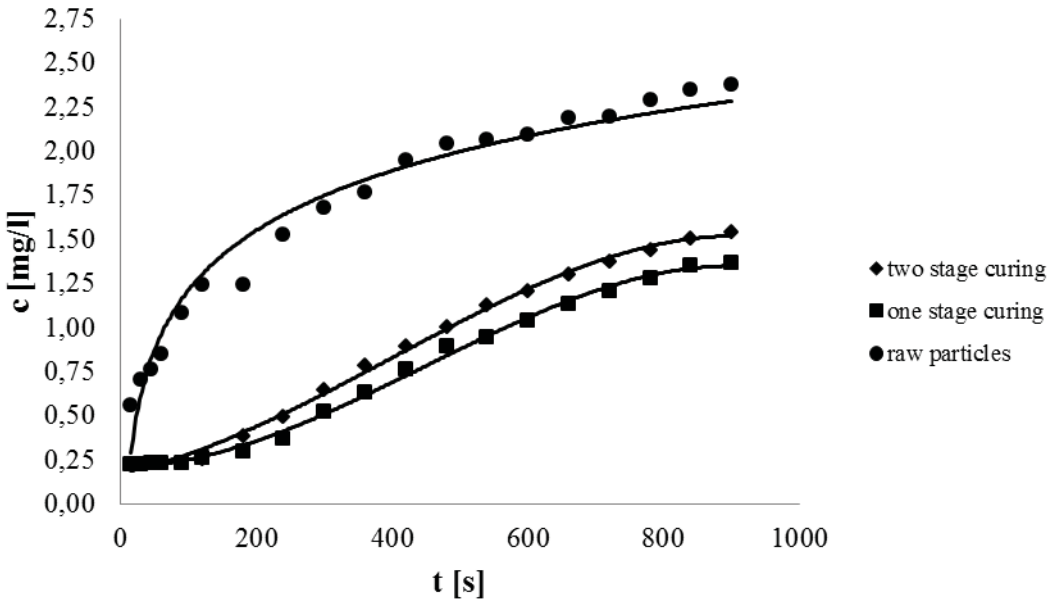

Fig. 8. Methylene blue concentration as a function of time for an example product obtained in the column (alkaline environment).

Two stage curing caused small drop of coating layer dissolution both in acidic and alkaline environments, but in acidic environment it stopped to dissolve practically after some specific time (constant concentration of the marker in time) (Fig.7 and Fig.8). The applied plasticizer quantity lowered glass transition temperature of AQOAT to the level, that the product curing could be obtained at low temperature in the column.

6. Conclusions

The apparatus, that was tested could be successfully applied for the dry coating of the intestine medicine. The obtained product is characterized by good strength in the conditions, that are in the stomach. The results of experiments show also, that some modification of the apparatus used in the examination is needed to lower the feedstock loss and particles agglomeration. Especially the bottom of the apparatus and the cone part with nozzles introducing powder and plasticizer should be modified.

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